

B<sup>1</sup> Nucleotide sequence and amino acid sequence analysis also revealed that sHVEM1, sHVEM2, and sHVEM3 have particularly high sequence identity with membrane-bound herpesvirus entry mediator (mHVEM), a member of the TNF receptor (TNFR) superfamily. For example, sHVEM1 displays 88.5% full length nucleotide sequence identity and 65.7% amino acid sequence identity with mHVEM, sHVEM2 displays 82.1% full length nucleotide sequence identity and 66.8% amino acid sequence identity with mHVEM, and sHVEM3 displays 56.7% full length nucleotide sequence identity and 65.4% amino acid sequence identity with mHVEM. However, the sHVEM1, sHVEM2, and sHVEM3 sequences differ from mHVEM sequence in two important ways. First, sHVEM1, sHVEM2, and sHVEM3 lack the C-terminal end of mHVEM (amino acids 185 to 283 of SEQ ID NO:13) which contains the transmembrane domain of mHVEM (amino acids 201 to 225 of SEQ ID NO:13). The absence of a transmembrane domain in sHVEM1, sHVEM2, and sHVEM3 suggests that sHVEM1, sHVEM2, and sHVEM3 act as soluble receptors. Secondly, sHVEM1, sHVEM2, and sHVEM3 have additional amino acids at their C-terminal ends that are not found at the C-terminal end of mHVEM, e.g., sHVEM1 contains an additional 10 amino acids at its C-terminal (amino acid 184 to 193 of SEQ ID NO:2), sHVEM2 contains an additional 14 amino acids at its C-terminal end (amino acid 184 to 197 of SEQ ID NO:18), and sHVEM3 contains an additional 2 amino acids at its C-terminal end (amino acid 185 to 186 of SEQ ID NO:30). Moreover, these amino acid sequences do not appear to have significant sequence identity with any other known protein.

Nucleotide sequence and amino acid sequence analysis also revealed that mHVEM2 has particularly high sequence identity with membrane-bound herpesvirus entry mediator (mHVEM), a member of the TNF receptor (TNFR) superfamily. For example, mHVEM2 displays 75.4% nucleotide sequence identity and 86.7% amino acid sequence identity with mHVEM. However, while mHVEM2 contains the mHVEM transmembrane domain (for mHVEM, amino acids 201 to 225 of SEQ ID NO:13; for mHVEM2, amino acids 203 to 225 of SEQ ID NO:42), mHVEM and mHVEM2 differ at their C-terminal ends, after amino acid 242 of SEQ ID NO:42. After amino acid 242, mHVEM and mHVEM2 share only one residue (at position 261), and otherwise differ from amino acids 243 to 277 of mHVEM2 (SEQ ID NO:42) and from 243 to 283 of mHVEM (SEQ ID NO:13).